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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HAGHIGHATIAN, MINA	
ART UNIT	**PAPER NUMBER**
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/804,710	DESTEFANO ET AL.	
	Examiner	Art Unit	
	MINA HAGHIGHATIAN	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09/05/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/05/08 has been entered.

Receipt is acknowledged of the Remarks filed on 09/05/08. No amendments have been filed. Accordingly, claims **1-7** remain pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification, while being enabling for albuterol sulfate and ipratropium bromide, does not reasonably provide enablement for all active ingredients. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to use the invention commensurate in scope with these claims.

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Formal, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re

Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

The nature of the invention, relative skill level, and breadth of the claims

The instant invention is directed to a formulation comprising water in an amount of from 0.13 to 0.18%, at least one HFA as propellant, one or more active ingredient and one or more excipients.

The complex nature of the claims is greatly exacerbated by the breath of the claims. The claims encompass any active ingredient.

The relative skill of those in the art is high, that of an MD or PHD.

The state and predictability of the art

As illustrative of the state of the art, the examiner cites Williams et al (Drug Development and industrial Pharmacy (provided in IDS filed on 01/29/08)) which indicates that different drugs have different solubilities and that moisture may influence the physical and chemical stability of the formulation. It is then concluded that different active compounds respond differently to the amount of moisture available in the system. Therefore William et al. indicates that generalizations cannot be made for all active compounds and the amount of water required to prepare a stable formulation. (see Discussion, page 77).

The amount of direction or guidance provided and the presence or

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[1] As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

absence of working examples

The specification provides no direction or guidance for how to prepare stable formulations comprising different active compounds (other than albuterol sulfate and ipratropium bromide). Due to the vastness of compounds available for such formulations, one of ordinary skill would undergo undue experimentation in deducing which compounds can actually be stable at the given water content. Furthermore, claims 1 and 2 are directed to formulations comprising any active ingredient and 0.13 to 0.18% water. Applicant has not shown that such claim can be made.

Thus, in the absence of working examples there is no showing that any active ingredient will form a stable formulation at water levels of 0.13 to 0.18%. Since it is clear that not all active compounds can be in a stable formulation with the given amount of water, additional direction or guidance is needed to make and use the invention as claimed and the specification has no such direction or guidance.

The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the all active compounds will be in a stable formulation containing 0.13 to 0.18% water, as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adjei et al (US 6,261,539).

Adjei et al teach medicinal formulations containing a particulate drug, a propellant and a stabilizing agent comprising a water addition (see abstract and col. 2, lines 42-45). Suitable medicaments include albuterol and ipratropium bromide (see col. 2, lines 54-58). Suitable propellants include HFA 134a and HFA 227 (see col. 3, lines 32-45). Suitable stabilizer is a water addition (see col. 3, line 47-58). It is also disclosed that generally the formulation comprises about 300 ppm after and an amount of from 300 to 2000 ppm water is added as a stabilizer (col. 4, lines 8-20 and claim 7). Suitable co-

solvent is ethanol (see col. 2, lines 30-33). Conventional lubricants, surfactants and co-solvents can be added (col. 4, lines 34-38).

Adjei also discloses that "An aerosol formulation preferably comprises the water addition in an amount effective to stabilize the formulation relative to an identical formulation not containing the water addition i.e. containing only nascent formulation water, such that the drug does not settle, cream of flocculate after agitation so quickly as to prevent reproducible dosing of the drug (see col. 3, lines 59-65). Adjei further discloses that the water addition must be present in a formulation in an amount in excess of the concentration of the nascent formulation water (see col. 4, lines 8-29).

While Adjei does not anticipate the claimed formulation because the specific range of water is not disclosed, Adjei teaches the same formulations and that addition of a small amount of water to the formulations provides stability to the formulations. The water is added as a stabilizer. The claimed concentration range of 0.13 to 0.18% is within the disclosed range of 0.03 to 0.2% (300 to 2000 ppm). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have selected the suitable amount of water as disclosed by Adjei according to the active agent and other excipients in the formulation. Thus, regarding the claimed ranges, it is considered that where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. See MPEP 2144.05 [R-5].

It has also been decided that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges

by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969); Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed.Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). See MPEP 2144.05.

Claims 1-4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lewis et al (EP 1219293).

Lewis et al teach a composition for use in an aerosol inhaler comprising an active agent, an HFA propellant and a cosolvent. Cosolvents include alcohols such as **ethanol** and propellants include HFA 134a and HFA 227 (see [0012] and [0010]). The active agents may be any one or more salbutamol (also known as albuterol), ipratropium bromide, beclomethasone, etc (see [0064]). The formulations may include a low volatility component such as **polyvinyl pyrolidone** (see 0056]). Other suitable low volatility materials include saturated and unsaturated carboxylic acids such as ascorbic acid (see [0055]).

Lewis also discloses the method of making the formulation and filling the aerosol inhaler. The method includes filling the container with a) one or more active materials, b) One or more low volatility components, c) One or more co-solvents followed by the addition of the HFA propellant. The formulations are said to contain up to 0.5% water and Table 2, discloses four formulations two of which contain **0.1% water**.

While Lewis et al does not anticipate the claimed formulation because the specific range of water is not disclosed, Lewis et al teach the same formulations and that addition of a small amount of water to the formulations provides stability to the formulations. Lewis et al teach the broader range of up to 0.5% and exemplify formulations that contain 0.1%. The cited "0.1%" by Lewis et al could potentially be the rounded amount of 0.1 to <0.2%, which includes 0.13 to 0.18%. Even if this is not the interpretation given to the disclosure, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have selected the suitable amount of water as disclosed by Lewis et al according to the active agent and other excipients in the formulation. Thus, regarding the claimed ranges, it is considered that where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. See MPEP 2144.05 [R-5].

It has also been decided that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of

scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969); Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed.Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). See MPEP 2144.05.

Claims 1-4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ashurst et al (6,511,652).

Ashurst et al teach a metered dose inhaler having part or all of its internal surfaces coated with one or more fluorocarbon polymers for dispensing an inhalation drug formulation comprising beclomethasone dipropionate, a propellant in combination with other active agents and one or more excipients (see abstract and summary). The co-solvent is preferably an alcohol such as **ethanol** (col. 2, lines 60-66). Suitable active agents include **salbutamol, ipratropium**, etc or combinations thereof. Suitable propellants include **HFA 134a or HFA 227** (col. 3, lines 5-50).

Ashurst et al also discloses that the said formulation preferably contain at least 0.015%, e.g. 0.015 to 0.1% water by weight of the formulation (col. 5, lines 24-39).

While Ashurst et al does not anticipate the claimed formulation because the specific range of water is not disclosed, Ashurst et al teach the same formulations and the addition of a small amount of water to the formulations. Ashurst et al teach the broader range of at least 0.015% and exemplify formulations that contain 0.015 to 0.1%. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have selected the suitable amount of water as disclosed by Ashurst et al according to the active agent and other excipients in the formulation. Thus, regarding the claimed ranges, it is considered that where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. See MPEP 2144.05 [R-5].

It has also been decided that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969); Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed.Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). See MPEP 2144.05.

Claims 1-4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Keller et al (6,475,467).

Keller et al teach suspension formulations for delivery by metered dose inhalers comprising active agents in particulate form. It is disclosed that in such formulations the amount of **water** is less than 1% by weight (see col. 3, lines 55-67). The active agents suitable for the said formulations include ipratropium bromide, salmeterol, mometasone, etc. Formulations may comprise **two or more active agents** (col. 5, lines 20-45). Examples of preferred co-solvents include **ethanol** (col. 9, lines 1-10). Formulations may contain a buffer substance such as **citric acid** (col. 9, lines 29-35). Suitable propellants include HFA 134a and HFA 227 (col. 7, lines 54-60).

Keller et al does not anticipate the claimed formulation because the specific range of water is not disclosed, however, Keller et al's formulation comprise less than 1% water. While the range of less than 1% is a broader range compared to the specific range of 0.13 to 0.18% as claimed, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have selected the suitable amount of water as disclosed by Keller et al according to the active agent and other excipients in the formulation. Thus, regarding the claimed ranges, it is considered that where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. See MPEP 2144.05 [R-5].

It has also been decided that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges

by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969); Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed.Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). See MPEP 2144.05.

Claims 5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adjei et al in view of Jager et al (WO 9413262).

Adjei et al, discussed above, lacks specific disclosure on addition of citric acid.

Jager et al teach stabilized medicinal aerosol solution formulations comprising medicaments that degrade or decompose by interaction with solvents or water, an HFC propellant, a cosolvent and an acid (see abstract). Most preferred medicaments for use in the said aerosol solution formulations include **ipratropium bromide and albuterol** (see page 8, lines 3-8). The suitable cosolvents include ethyl alcohol, polyethylene glycol, glycerol, etc. Most preferred cosolvent is **ethanol** (see page 9, line 17 to col. 10, line 11). The disclosed formulations contain an acid to prevent degradation. Suitable acids include ascorbic acid and **citric acid**, and the most preferred acid is citric acid

(page 10, lines 17-32). Table 1 discloses a formulation comprising ipratropium bromide monohydrate, ethanol, HFA 134a, acid and water in the amount of 0.0 to 5%.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have combined formulations and method of making them as taught by Adjei et al and Jager et al and end up with the claimed formulations. Alternatively, it would have been obvious to one of ordinary skill in the art given the general teachings of Adjei et al on the formulations, to have looked in the art for other suitable excipeints such as stabilizers like, citric acid as taught by Jager et al with the reasonable expectations of successfully preparing stable and effective formulations for aerosol administration. In other words, all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Claims 5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lewis et al (EP 1219293) in view of Jager et al (WO 9413262).

Lewis et al and Jager et al are discussed above. Lewis et al discloses all the components of the instant claims except for citric acid. While disclosing addition of carboxylic acids such as ascorbic acid, lacks specific disclosure on citric acid.

Jager et al teaches the addition of an acid such as citric acid to the formulations as a stabilizer and a buffer.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have combined formulations and method of making them as taught by Lewis et al and Jager et al and end up with the claims formulations. Alternatively, it would have been obvious to one of ordinary skill in the art given the general teachings of Lewis et al on the formulations and method of making them, to have looked in the art for specific carboxylic acids such as citric acid as taught by Jager et al with the reasonable expectations of successfully preparing stable and effective formulations for aerosol administration. In other words, the claims would have been obvious because a person of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention and that there would have been a reasonable expectation of success.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims **1-7** are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,423,298 in view of Adjei et al (US 6,261,539). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant Application would have been obvious over the claims of the U.S. Patent '298 in view of Adjei et al '539. Specifically, the instant claims and the reference claims are drawn to a formulation comprising an HFA propellant, one or more active agents and one or more excipients. The instant claims additionally require 0.13 to 0.18% water and reference claims do not require water. Adjei et al discloses similar formulations and teaches that the addition of a small amount of water from 300 to 2000 ppm, would improve stability of the formulations. Thus it would have been obvious to one of ordinary skill in the art to have implemented the teachings of Adjei e et al on water addition, as a stabilizer in the formulations of the reference claims with a reasonable success.

Response to Arguments

Applicant's arguments filed 09/05/08 have been fully considered but they are not persuasive.

Applicants main argument appears to be that none of the references applied in the rejection of claims 1-7 teach the specific water concentration range of 0.13 to 0.18%. Applicant then concludes that none of the references can properly anticipate the narrow range of the instant claims. The arguments are combined with a Declaration by George Destefano. The Declaration provides data obtained from various experiments done on albuterol sulfate and ipratropium bromide. Each experiment comprises a different amount of water. In concluding Mr. Destefano argues that the data shows that formulations comprising 1500 ppm or greater (equivalent to 0.15%) water is needed to ensure that the single actuation reproducibility difference does not impact the product. In other words, water content of less than 1200 ppm resulted in poor reproducibility, while water content of 1500 to 2500 ppm (equivalent to 0.15 to 0.25%) exhibited good results (see Declaration, page 2). This is not persuasive, 1) because the argued preferred range is within the range of prior art such as Adjei (300-2000 ppm). Thus Adjei's upper limit meets the limitation of claimed range. Also Adjei discloses adding the said amount of water to the nascent water already in the formulation. 2) While the two Figures (2 and 3) show that the range of 1500 to 2500 ppm water produces better results, the remaining data does not support applicants assertion. For better illustration, we can look at three tables, each showing a different water content. Table for AS No. 02-10-7501 has a water content of much lower than 1500 ppm. At 25 actuation, Can 1, the number for albuterol is 115.13 and for ipratropium it is 20.56. The same numbers for a water content of 2500 ppm (AS No. 02-10-7506), are 118.31 and 20.22 respectively. The same numbers for a water content of 3500 ppm (AS No. 02-10-7508) are 119.26

and 21.31. There is no significant difference between, for example, 115.13, 118.31 and 119.26 (for albuterol). There is even less distinction shown between 20.56, 20.22 and 21.31 (for ipratropium). Thus it is the Examiner's position that no unexpected results shown and that references teaching a water content the overlaps the cited ranges meets the claim ranges.

Claims 1-7 remain rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINA HAGHIGHATIAN whose telephone number is (571)272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mina Haghighatian/

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